

Appl. No. : 10/687,523  
Filed : October 15, 2003

### REMARKS

The Specification has been amended to remove the references to the browser-executable codes. Claim 12 has been amended. Support for the amendment can be found in original claims 6-9 and in paragraphs [0033]-[0035] of the Specification as filed. Therefore, no new matter has been introduced by these amendments. The following addresses the substance of the Office Action.

#### Specification

The Examiner has objected to the Specification for reciting embedded hyperlinks in paragraphs [0011] and [0015]. Applicant has amended the Specification accordingly.

#### Compliance with 35 USC §112

The Examiner has rejected Claims 12-17 under 35 USC §112, second paragraph, as being allegedly indefinite. More specifically, Claim 12 was found indefinite for not reciting a reference to SEQ ID NO: for amino acid position 481. Applicant respectfully disagrees. Since the entire amino acid sequence of human ClCKb is published in GenBank NCBI under accession number NM\_000085 (see paragraph [0011] of the Specification as filed), a skilled person would know exactly where position 481 is located in the whole protein. Therefore, there is no need to recite the SEQ ID NO in Claim 12. Furthermore, information explaining precisely what is meant by a polypeptide derived from ClCKb protein and having a genetic alteration at amino acid position 481 is given in paragraph [0014] of the Specification as filed. The Specification clearly states that instead of using the entire genetically altered ClCKb protein, the invention can be successfully performed using a segment of the ClCKb protein as long as this segment (polypeptide) is covering an amino acid position which corresponds to position 481 of the full protein. Claim 12 has been amended to clarify that the polypeptide comprises an amino acid corresponding to amino acid at position 481 in the ClCKb protein. Therefore, Claim 12 is definite.

The Examiner further stated that the term "peptide" recited in Claim 12 is art-recognized as being less than 100 amino acids in length, and that according to the PTO's own classification a peptide is less than 100 amino acids. Therefore, a peptide would not be expected to have a chloride channel activity as recited in Claim 15, which requires a large protein spanning membranes 10-12 times. Therefore, the Examiner has additionally found Claims 15-17 as

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lacking antecedent basis in Claim 12. Applicant respectfully disagrees. The art-recognized meaning of the term “peptide” is “two or more amino acids joined by a peptide bond”, i.e., short peptides of less than 100 amino acids, long peptides of more than 100 amino acids, and large proteins comprising thousands of amino acids (see Appendices 1 and 2). Therefore, Claims 12-17 as filed are definite. However, to comply with the PTO’s definitions of the terms “peptide” and “polypeptide”, Applicant has amended Claim 12 to now recite the term “polypeptide”. Support for this amendment can be found, for example, in paragraphs [0033]-[0035] of the Specification as filed. Therefore, the amended Claim 12, as well as Claims 13-17 are definite, and Claims 15-17 have antecedent basis in Claim 12.

Additionally, the Examiner has requested that the abbreviation “CLICKb” in Claim 12 is spelled out. Applicant has amended Claim 12 to spell out “chloride channel Kb”. Support for this amendment can be found in paragraph [0011] of the Specification as filed.

Therefore, Claims 12-17 are definite, and their rejection under 35 US §112, second paragraph should be withdrawn.

The Examiner has rejected Claims 12-17 under 35 USC §112, first paragraph as allegedly lacking written description. More specifically, the Examiner alleges that there is no written description regarding how to measure ion conductance across membranes comprising a peptide of less than 100 amino acids derived from CLICKb and comprising the T481S mutation. Applicant respectfully disagrees. Claims 12-17 do not limit the length of the claimed peptide to less than 100 amino acids. As discussed above, the term “peptide” is broad and covers full-length proteins, long fragments thereof of more than 100 amino acids, as well as short fragments of less than 100 amino acids. Therefore, Claims 12-17 as filed have support in the specification as filed. However, as discussed above, to comply with the US PTO’s own definition of the term “peptide”, applicant has now amended Claim 12 to recite the term “polypeptide”. The polypeptide is expected to have chloride ion channel activity. Therefore, Claims 12-17 as amended are supported by the Specification as filed, and their rejection under 35 USC §112, first paragraph should be withdrawn.

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### CONCLUSION

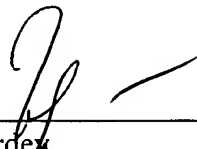
Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefor, and arguments in support of the patentability of the pending claim set are presented above. Any claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: June 20, 2005

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# APPENDIX 1

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# peptide

(Science: biochemistry) A compound of two or more amino acids where the alpha carboxyl group of one is bound to the alpha amino group of another.

Amide combining the amino group of one amino acid with the carboxyl group of another; usually obtained by partial hydrolysis of protein.

Any compound consisting of two or more amino acids.

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# APPENDIX 2

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peptide

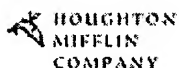


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[Dictionary](#)  
pep·tide (pěp'tīd')   
*n.*

Any of various natural or synthetic compounds containing two or more amino acids linked by the carboxyl group of one amino acid to the amino group of another.

[PEPT(ONE) + -IDE.]

pep·tid'ic (-tīd'īk) *adj.*  
pep·tid'i·cal·ly *adv.*

**Columbia  
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Press**



[Encyclopedia](#)  
peptide, organic compound composed of [amino acids](#) linked together chemically by peptide bonds. The peptide bond always involves a single covalent link between the  $\alpha$ -carboxyl (oxygen-bearing carbon) of one amino acid and the amino nitrogen of a second amino acid. In the

formation of a peptide bond from two amino acids, a molecule of water is eliminated. Small peptides with fewer than about ten constituent amino acids are called oligopeptides, and peptides with more than ten amino acids are termed polypeptides. Compounds with molecular weights of more than 10,000 (50–100 amino acids) are usually termed proteins. Organisms commonly contain appreciable quantities of low-molecular-weight peptides some arising from proteins while others are synthesized directly. Certain of these molecules are unusual in that they incorporate amino acids not found in proteins such as amino acids of the D-configuration. Among the biological peptides are many with physiological or antibacterial activity, such as the peptide hormones oxytocin and vasopressin; adrenocorticotrophic hormone (ACTH), secreted by the pituitary gland; and several cyclic peptides, in which the amino-acid sequence forms a ring structure rather than a straight chain, such as the antibiotics tyrocidin and gramicidin. Laboratory synthesis of peptides has risen to the level of a well-defined art in recent years. Synthetic peptides, composed of as many as a hundred amino acids in specified sequence, have been prepared in the laboratory with good purity and high yields.



### Medical

pep·tide (pěp'tīd')

*n.*

Any of various natural or synthetic compounds containing two or more amino acids linked by the carboxyl group of one amino acid and the amino group of another.

pep·tid'ic (-tīd'ik) *adj.*

pep·tid'i·cal·ly *adv.*



### WordNet

*Note: click on a word meaning below to see its connections and related words.*

The *noun* peptide has one meaning:

Meaning #1: amide combining the amino group of one amino acid with the carboxyl group of another; usually obtained by partial hydrolysis of protein



### Wikipedia

peptide



**Peptides** (from the Greek *πεπτος*, "digestable"), are the family of molecules formed from the linking, in a defined order, of various amino acids. The link between one amino acid residue and the next is an amide bond, and is sometimes referred to as a peptide bond. An amide bond is somewhat shorter than a typical carbon-nitrogen single bond, and has a partial double-bond character, because the participating carbon atom is doubly bonded to an oxygen atom and the nitrogen has a lone pair of electrons available for bonding.

Peptides (like proteins) occur in nature and are responsible for a wide array of functions, many of which are not yet understood. Antimicrobial peptides generally disrupt the membranes of a target cell, causing lysis of the cell. How this occurs, and what determines the activity and selectivity of these peptides, is currently only known approximately.

It has also been documented that when certain food proteins such as gluten, casein, egg protein and spinach protein are broken down, opioid peptides are formed. These peptides mimic the effects of morphine, and those who are unable to break them down will experience mental illness. These peptides are quite short and are given names such as casomorphine, gluten exorphine and dermorphine.

Peptides differ from proteins, which are also long chains of amino acids, by virtue of their size. Traditionally, those peptide chains that are short enough to make synthetically from the constituent amino acids are called peptides rather than proteins. The informal dividing line is at approximately 50 amino acids in length (some people claim shorter lengths), since naturally-occurring proteins tend, at their smallest, to be hundreds of residues long. So, in essence, *a peptide is a small protein*.

There is considerable movement to redefine this arbitrary distinction such that a peptide is an amino acid molecule without structure; on gaining defined structure it is a protein. Thus the same molecule can be either a peptide or a protein depending on its environment; though there are often peptides which cannot be proteins.

Peptidomimetics (such as peptoids and  $\beta$ -peptides) are molecules related to peptides, but with different properties.

### The Grand Peptide Families

#### Vasopressin and Oxytocin

- Vasopressin
- Oxytocin

#### The Tachykinin Peptides

- Substance P
- Kassinin